instant invention. This alignment can be found on pages 2-3 of Appendix A (identical residues are shaded). The presence of two PDI catalytic sites and an ER-retention signal clearly suggest that the protein is related to the PDI family. When the amino acid sequence of the instant SEQ ID NO:10 was compared with those of the usual type of PDI identified in alfalfa (GI 266743; Shorrosh et al. of record), maize (GI 1709619; Li et al. of record), wheat (GI 1709620; Shimoni et al. of record) and *Arabidopsis* (GI 2708314 of the instant application; GI 9759328; GI 12323392), it is clear from the results in Appendix A that they all contain the two active-site motifs of thioredoxin (Trp-Cys-Gly-His-Cys; -WCGHC-) and they are located in the endoplasmic reticulum (Lys-Asp-Glu-Leu; -KDEL-) (see boxed amino acids). Please note that the amino acid sequences of the two active site regions are highly conserved, but the amino acid sequences outsides those regions are poorly conserved even between well-known PDIs (i.e., the percent identity of two *Arabidopsis* PDIs is only 34.8% - GI 2708314 and GI 9759328).

Furthermore, Applicants also bring the article entitled "Active Site Peptides with CXXC Motif on MAP-Resin can Mimic Protein Disulfide Isomerase Activity" , submitted herewith, to the Examiner's attention (Ookura et al., *Biochem. Biophys. Res. Comm.* 213(3):746751 (1995), hereinafter "Ookura et al."). In their study, Ookura et al. attempted to mimic the PDI activity with active site peptides. Ookura et al. state that (APWCGHCK)8-MAP peptide (hereinafter "MAP-peptide") exhibited a PDI activity a thousand times lower than bovine PDI, but were comparable to that of thioredoxin, a protein with PDI-like activity. Ookura et al., page 748, third full paragraph. Ookura et al. further state that in contrast to the MAP-peptide, mono-molecular peptides, APWCGHCK and APWCGPCK, did not exhibit any PDI activity. Ookura et al., page 749. This finding is, in part, ascribed to the fact that the APWCGHCK peptides on the MAP-peptide are in closer proximity than free APWCGHCK peptides in solution (mono-molecular peptides) and that such a proximity is conducive to the formation of an active site configuration through disulfide bridge(s). Ookura et al., page 749, second full paragraph. In the subject invention, SEQ ID NO:10 does has its two active sites in appropriate proximity, comparable to the MAP-peptide.

Applicants state that the claimed invention is directed to SEQ ID NO:10 possessing a PDI activity. The alignment of SEQ ID NO:10 with known PDIs and the work of Ookura et al. establishes the necessary burden of proof required in the Guidelines for Examination of Patent Applications under the "Written Description" Requirement (hereinafter "Guidelines"). In its Guidelines, the PTO has determined that the written description requirement can be met by "show[ing] than an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics.....

i.e., complete or partial structure, other physical and or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure or some combination of such characteristics." Guidelines, 66 Federal Register at 1106 (emphasis added). Weighing all factors, 1) that the full length open reading frame (SEQ ID NO:10) is disclosed, and 2) the correlation between structure and function of the genes, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the Applicants were in possession of the claimed invention which comprises SEQ ID NO:10.

In view of the above discussion, withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, is respectfully requested.

The Examiner maintains that claims 16-20, 22-30 and 36-38 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons set forth in the Office Action mailed June 29, 2001, Paper No. 10. The Examiner states that although a citation of an assay for measuring enzyme activity was part of the instant invention, no activity data has been provided for the claimed compounds. Applicants traverse this rejection.

The law is well settled that there is no absolute statutory requirement that the specification contain a working example if the disclosure is such that one skilled in the art can practice the claimed invention. *In re Borkowski*, 164 USPQ 642 (CCPA 1970). Furthermore, claim 16 recites two physiochemical properties of the claimed polynucleotides. Specifically, this claim recites (1) a specific sequence identity and (2) a function limitation (i.e., enzymatic activity). At the time the claimed invention was made, one of skill in the art could determine, without undue experimentation, whether a polynucleotide falls within the scope of claim 16 by simply comparing the amino acid sequence encoded by this polynucleotide with the amino acid sequence of SEQ ID NO:10 recited in claim 16, and by transforming cells with an expression cassette containing the polynucleotide and assaying the transformed cells for enzymatic activity with that assay that is cited in the instant invention. Although these tasks may be time consuming, they do not defeat patentability. It is submitted that claim 16 and the other pending claims are fully enabled.

In view of the above discussion, withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph, is respectfully requested.

New Rejections:

Claim Rejections - 35 U.S.C. § 101

Claims 16-20, 22-30 and 36-38 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Applicants respectively traverse.

The Examiner, in essence, asserts that the assignment of protein disulfide isomerase to the disclosed plant polynucleotide is not credible. Applicants note that biochemical data is not mandated by the law in order for the utility requirement to be met. Computational biological data are as good as any other type of data in supporting a functional assignment. Applicants refer to the specification as filed, Table 6, beginning on page 21, line 28, which shows the percent identity of amino acid sequences deduced from the nucleotide sequences of cDNA clones encoding polypeptides homologous to RB60 (protein disulfide isomerase).

The references cited in the Office Action in support of the 101 rejection are one to four years prior to the priority date claimed by Applicant for the subject application. It is not disputed that the level of skill in the art was high at the time the claimed invention was made. In addition, the level of skill in the art advanced, particularly within four years, to overcome the challenges set forth in the cited references.

In addition, Applicants hereby incorporate by reference the remarks set forth above (regarding 35 U.S.C. § 112, first paragraph), for the sake of brevity, and Appendix A. The alignment in Appendix A provides guidance to the catalytic domain essential for PDI activity in SEQ ID NO:10. Thus, the claimed invention is supported by well established utility (i.e., SEQ ID NO:10 may be used for hybridization purposes since the encoded protein has utility as a PDI). Applicants note that the record as a whole provides an asserted utility for the claimed invention that is specific and would be considered credible be a person of ordinary skill in the art.

In view of the above discussion, withdrawal of the rejection of the claims under 35 U.S.C. § 101, first paragraph, is respectfully requested.

Conclusion

In view of the amendments and remarks above, Applicants respectfully submit that the application is in condition for allowance. Early and favorable notification of allowance of claims 16-20, 22-30 and 36-38 is earnestly solicited. The Examiner is invited to contact the undersigned if there are any questions concerning the prosecution of this application.

The Commissioner is authorized to charge Deposit Account No. 04-1928 (E. I. du Pont de Nemours and Company) for any fees necessitated by this response.

Respectfully submitted,

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